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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/541,901

06/16/2006

Joseph Strauss

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EXAMINER

JOIKE, MICHELE K

ART UNIT

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1636

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/541,901	Applicant(s) STRAUSS ET AL.	
	Examiner MICHELE K. JOIKE	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-7 and 14-31 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-7 and 14-31 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 11 July 2005 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>5/11/06, 5/12/06</u> | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-7 and 14-31 are pending and examined.

Specification

The disclosure is objected to because of the following informalities: This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 because sequences were set forth that lack sequence identifiers. These sequences include the sequences listed in the claims and throughout the specification. Nucleotide sequences with 10 or more nucleotides and amino acid sequences with 4 or more amino acids require sequence identifiers. If the Sequence Listing required for the instant application is identical to that of another application, a letter may be submitted requesting transfer of the previously filed sequence information to the instant application. For a sample letter requesting transfer of sequence information, refer to MPEP § 2422.05. Additionally, it is often convenient to identify sequences in figures by amending the Brief Description of the Drawings section (see MPEP § 2422.02).

Page 20 contains a nucleotide sequence without a sequence identifier.

Applicants are required to comply with all of the requirements of 37 CFR 1.821 through 1.825. Any response to this office action that fails to meet all of these requirements will be considered non-responsive. The nature of the noncompliance with the requirements of 37 C.F.R. 1.821 through 1.825 did not preclude the continued

examination of the application on the merits, the results of which are communicated below.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 6 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that the vectors, pRM2085, pRM2124, pRM2119, pERE URA JUNK, pERE URA nirA and pERE JUNK nirA, are required to practice the invention. As such, the vectors must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the vectors. In the instant case, the process to generate the vectors that is disclosed in the specification does not appear to be repeatable, nor does it appear the vectors are readily available to the public.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may

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provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

- a) during the pendency of the application, access to the invention will be afforded to the

Commissioner upon request;

- b) all restrictions upon availability to the public will be irrevocably removed upon the granting of the patent;

- c) the deposit will be maintained in a public depository for a period of 30 years, or 5 years after the last request for the enforceable life of the patent, whichever is longer;

- d) a test of the viability of the biological material at the time of deposit (see 37 CFR 1.807); and

- e) the deposit will be replaced if it should ever become inviable.

Failure to make one of the preceding indications in response to this Office Action will result in the rejection being maintained in either a second Non-Final or a Final rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4 and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Metzger et al.

Metzger et al (Nuc. Acid Res. 20(11): 2813-2817, 1992, specifically p. 2813, Figures 1 and 2) teach expression cassettes in yeast. One expression cassette contains the estrogen receptor with has two transcriptional activation domains. The other expression cassette contains either the chimeric GAL1 or URA3 promoters which are estrogen-responsive. The promoter is operatively linked to a LacI-LacZ gene construct. The estrogen receptor is also operatively linked to a promoter, in that the receptor binds the promoter to stimulate transcription. Metzger et al show that the estrogen receptor is able to stimulate transcription in yeast in the presence of estrogen. Figure 2 shows that no estrogen results in zero β -galactosidase activity, but adding 0.5 nM or higher will result in β -galactosidase activity. Also taught is modulating gene expression in yeast by inducing the LacI-LacZ gene expression cassette by adding estrogen to activate the receptor binding to the chimeric estrogen promoter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Parks et al.

Claim 5 requires that the promoter comprises a stuffer fragment.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a stuffer fragment.

Parks et al (J. of Virology 73(10): 8027-8034, 1999, specifically pp. 8027 and 8032) teach the use of a stuffer fragment in a vector for use in cloning.

The ordinary skilled artisan, desiring to use a stuffer fragment, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system with the teachings of Parks et al teaching use of a stuffer fragment in a vector because Parks et al state that stuffer DNA can significantly improve gene expression. It would have been obvious to one of ordinary skill in the art to use a stuffer fragment because Parks et al teach that stuffer DNA helps maintain vector size, and it would follow that the a certain desired promoter size could also be maintained by a stuffer fragment. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 7, 18, 21 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Blinkovsky et al.

Claims 7, 18, 21 and 27 claim the filamentous fungus is *Fusarium venenatum*.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a steroid inducible promoter expression system in *Fusarium venenatum*.

Blinkovsky et al (Appl. and Env'tl. Micro. 65(8): 3298-3303, 1999, specifically pp. 3298 and 3302) teach the using *Fusarium venenatum* for heterologous expression.

The ordinary skilled artisan, desiring to use *Fusarium venenatum*, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system in a filamentous fungus with the teachings of Blinkovsky et al teaching using *Fusarium venenatum* for heterologous expression because Blinkovsky et al state that previous studies have shown that this organism has been able to produce a variety of recombinant enzymes. It would have been obvious to one of ordinary skill in the art to use *Fusarium venenatum* because Blinkovsky et al teach that *Fusarium venenatum* has low background levels of proteases is advantageous for the production of relatively pure enzyme products. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 14, 19, 22, 23, 28 and 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Gellissen et al.

Claims 14, 19, 22, 23, 28 and 29 claim the yeast is *Pichia pastoris* or *Hansensula polymorpha*.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a steroid inducible promoter expression system in *Pichia pastoris* or *Hansensula polymorpha*.

Gellissen et al (Appl. Micro. Biotech 54: 741-750, 2000, specifically pp. 741 and 746) teach heterologous protein production in methylotrophic yeast, specifically *Pichia pastoris* and *Hansensula polymorpha*.

The ordinary skilled artisan, desiring to use *Pichia pastoris* or *Hansensula polymorpha*, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system in a yeast with the teachings of Gellissen et al teaching heterologous protein production in methylotrophic yeast, specifically *Pichia pastoris* and *Hansensula polymorpha* because Gellissen et al state that the *Pichia pastoris* and *Hansensula polymorpha* systems have been well-established and utilized in especially competitive and consistent industrial-scale processes. It would have been obvious to one of ordinary skill in the art to use *Pichia pastoris* or *Hansensula polymorpha* because Gellissen et al teach that *Hansensula polymorpha* has the ability to co-express different genes in fixed, stable ratios which makes it attractive for the bioconversion of specific substrates into valuable industrial

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compounds. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 7, 18, 20 and 26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Harkki et al.

Claims 7, 18, 20 and 26 claim the filamentous fungus is *Trichoderma reesei*.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a steroid inducible promoter expression system in *Trichoderma reesei*.

Harkki et al (IDS ref. CM, specifically pp. 596) teach expression of bovine chymosin in *Trichoderma reesei*.

The ordinary skilled artisan, desiring to use *Trichoderma reesei*, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system in a filamentous fungi with the teachings of Harkki et al teaching expression of bovine chymosin in *Trichoderma reesei* because Harkki et al state that this fungus has considerable potential as a host for the production of heterologous mammalian proteins. It would have been obvious to one of ordinary skill in the art to use *Trichoderma reesei* because Harkki et al teach that filamentous fungi have long been used as commercial production organisms for a variety of enzymes and pharmaceuticals. Given the teachings of the prior art and the level of the ordinary

skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 14, 19, 24 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Swinkels et al.

Claims 14, 19, 24 and 30 claim the yeast is *Kluyveromyces lactis*.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a steroid inducible promoter expression system in *Kluyveromyces lactis*.

Swinkels et al (Antonie van Leeuwenhoek 64: 187-201, 1993, specifically pp. 187 and 198) teach heterologous gene expression in *Kluyveromyces lactis*.

The ordinary skilled artisan, desiring to use *Kluyveromyces lactis*, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system in a yeast with the teachings of Swinkels et al teaching heterologous gene expression in *Kluyveromyces lactis* because Swinkels et al state that *K. lactis* has excellent fermentation characteristics on large scale. It would have been obvious to one of ordinary skill in the art to use *Kluyveromyces lactis* because Swinkels et al teach that *Kluyveromyces lactis* successfully produces mammalian proteins with complex structures. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent

evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 14, 19, 25 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Metzger et al as applied to claims 1-4 and 15-17 above, and further in view of Kurtz et al.

Claims 14, 19, 25 and 31 claim the yeast is *Candida albicans*.

Metzger et al teach all of the limitations as described above, however, they do not teach use of a steroid inducible promoter expression system in *Candida albicans*.

Kurtz et al (Molecular and Cell Biol. 6(1): 142-149, 1986, specifically pp. 187 and 198) teach gene expression in *Candida albicans*.

The ordinary skilled artisan, desiring to use *Candida albicans*, would have been motivated to combine the teachings of Metzger et al teaching a steroid inducible promoter expression system in a yeast with the teachings of Kurtz et al teaching gene expression in *Candida albicans* because Kurtz et al teach that the presented transformation method is simple and rapid. It would have been obvious to one of ordinary skill in the art to use *Candida albicans* because Kurtz et al teach that the transformation method for *Candida albicans* will allow for new opportunities to study this medically important organism. Given the teachings of the prior art and the level of the ordinary skilled artisan at the time of the applicant's invention, it must be considered, absent evidence to the contrary, that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Allowable Subject Matter

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHELE K. JOIKE whose telephone number is (571)272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on 571-272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michele K Joike, Ph.D./

Michele K Joike, Ph.D.
Examiner
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